

## The Genetic Solution

### *How to Begin to Put the Knowledge of Genetics to Work for You*

*The final article in an occasional series on genomic and genetic medicine*

By DOUG SCOTT

OK, PAs, the gauntlet has been dropped and the challenge is now before you.

For the past two years, *AAPA News* has published articles about the importance of genetics, genomics, personalized medicine, family history, pharmacogenomics, genetic testing, the GINA bill, NCHPEG, EGAPP, and NHGRI among other topics. The question you may ask is: What is the clinical application for this science today?

Sometime in the near future a patient is going to come into your office for an appointment, and they are going to present you with a 31-page report from one of the three direct-to-consumer companies — Navigenics, 23andMe, and deCODEme — that provide spit test DNA analysis. This report is an analysis of their whole genome or what is called multiple single-nucleotide polymorphisms, or SNPs.

*To make the most of the [spit test DNA analysis] results, we encourage you to discuss your genetic insights with your [clinician].*

— Michael A. Nierenberg M.D.,  
medical director, Navigenics Inc.;  
from the *Navigenics Health Compass Report*, which is provided to patients.

The report itself is going to look at the genetic risk factors for your patient associated with up to 22 chronic conditions for



which genetic scientists have been able to identify multiple genes. Some of these include: Alzheimer's disease, atrial fibrillation, Crohn's disease, glaucoma, cardiac disease, obesity, and stomach cancer. Depending on the company, these reports may or may not include single-gene conditions such as breast cancer — BRCA1 and BRCA2 — and Huntington's disease, because reliable genetic tests are available to determine if a patient has those risk factors.

The report will automatically flag any disease for which the patient's lifetime risk is estimated to be greater than 25 percent, regardless of whether the average population risk is greater than 25 percent, and any disease where there is more than a 20 percent change in risk from the general population. For instance, if the average lifetime risk for Crohn's disease is 0.58 percent and your patient's risk is 0.87 percent, this will be flagged as a 50 percent increase in risk.

The report then individually specifies

each chronic condition and breaks it down to the known gene identified; the known genetic risk markers for that disease; which genetic risk markers your patient was found to have; the odds ratio associated with each marker (based on some type of evidence, but unknown as to the validity of evidence); and an estimate of the percentage of the condition that may be caused by environment and how much may be caused by the genes. The report goes into sections including what the information means, early detection and surveillance, potential drug treatment, what the patient can do, what patients should tell their clinician, what the clinician should do, clinical trials, what's next, and more information.

#### **Finding Answers**

Many of you may watch the television program, "Deal or No Deal"; the challenge now before you is Risk or No Risk. Considering all the genetic information the patient is going to throw before you,

*Continued on next page*



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## *Continued from previous page*

combined with other factors such as family history, social history, environment, etc.; the question that you are going to be asked at that visit is: How much of a risk factor does your patient really have for these aforementioned chronic conditions? Are you going to have to answer all of that by the end of the 10 minute appointment? Will you even know where to begin?

To help you understand how to counsel your patient, Philadelphia University Program Director Michael "Rocky" Rackover recently had his spit test DNA analysis completed by Navigentics. Rackover graciously agreed to share key concepts from his report and use a hypothetical patient report with the PA profession as we visited a faculty PA for her evaluation, a genetic counselor, the dean of the Philadelphia University school of Science and Health, one of the country's leading geneticists, and first-year PA students from the Philadelphia University program.

Overall, Rackover was not surprised by his DNA analysis results, but he did have concerns about how an SNP analysis would be interpreted if explaining increased risk. He designed a hypothetical case scenario for his first-year PA students dealing with one of the two APOE risk markers for Alzheimer's disease; the report explained that a lifetime risk based on the report is 16 percent, with an average lifetime risk of 9 percent.

"Would I have expected this result? No, not at all," confessed Rackover. "Would I have had a little anxiety having to understand the result of a slight increased risk of Alzheimer's disease? Probably.

"I asked my wife [Eileen] what her concern would be if I had increased risk of Alzheimer's and she basically said that I don't have a family history of Alzheimer's and that I do forget a little bit, every now and then. But the bottom line is it did cause a little anxiety for her if it would have been a real result.

"What I learned is: The reason why this conversation was so important, is as a PA, you need to feel comfortable communicating this kind of risk counseling with your

patients because I believe it is going to be a big part of the future practice of medicine."

### **What Does a Health Care Provider Think?**

The first stop was with Rackover's faculty member and PA, Trinell Genga, who works in internal medicine with John M. Columbo, M.D., in addition to being assistant professor at the Philadelphia University PA Program. Rackover presented Genga with his DNA report.

"Should I be concerned with this report?" asked Rackover.

"I think that I would keep it on your radar screen but I would not let this [report] ruin your life and worry about it non-stop," said Genga. "You need to be aware of it and talk to a genetic counselor and see what they say but at the same time I think you have to be careful with this information and not let it scare you too much to the point of not doing things that you would normally.

"Now the good part about report is, hopefully what it tells you so far as the cardiac disease, the obesity, Crohn's disease, and atrial fibrillation go; that you should start to lead a healthier life. So as your PA, I will encourage you to exercise and eat healthier. I hope this kind of information also helps to take a more active role in your own health care."

What did Genga think of the report?

"I was able to scan through it but I could not read it word for word during the visit," she said. "It was pretty interesting but what most of it talks about is his risk markers and I am not exactly sure what these markers indicate; I am not trained in any of that information. I would refer Rocky to a genetic counselor."

### **What Does a Genetic Counselor Think?**

Next was a visit with Erynn Gordon, a senior genetic counselor with Coriell Personalized Medicine Collaborative, who presented her analysis to first-year PA students at Philadelphia University.

"The first important thing to remember when looking at report like this is that there is so much information, the temptation is to just rely on this by itself," said Gordon,

who is presently working to investigate the utility of this direct-to-consumer DNA information. "But what do we know of Rocky's family history, social history?

"With Crohn's disease for example, Rocky told us in his family history that he is Jewish and we know that people in the Jewish population have a much higher rate of Crohn's disease. So as his health care provider, I might say to him you are at an increased risk of Crohn's disease over the general population *if* that was the only factor that we were looking at.

"However, looking at his Navigentics report, I can see that he does not have the genetic variant associated with Crohn's disease in the general population. Having both of these pieces of information, rather than just one or the other, provides the most complete picture.

"So to counsel your patient, you have to know how to incorporate multiple factors such as what symptoms the patient's having, what their lab results look like, what does the genetic DNA test say, what does the family history show, and all of those are equally important; you cannot just rely on one more than another."

Two key initial steps Gordon said PAs should consider when confronted with a spit test DNA analysis is to first consider asking the patient if you can study the test and get back to them at their next visit and the second is to know when to refer your patient to genetic counselor to evaluate the information.

"In my opinion it is always better to say to a patient: I am going to look it up, review this more thoroughly, and get back to you because the genetics that we are talking about are not medical emergencies," said Gordon. "This is not an emergency, unless something really jumps off the page and you need time to review it.

"Knowing when to refer a patient to a genetic counselor really depends on the patient, how comfortable you are with genetics, and how well you think the genetic counselor can answer the patient's questions," Gordon said. So you really have to recognize what your patient is comfortable

*Continued on next page*



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# AAPA News

April 15, 2009

## *Continued from previous page*

with, what your own limitations and knowledge of genetics are, and when you feel like you have done as much as you can and then refer them to a genetic counselor.”

Gordon said the second thing that PAs need to consider is explaining risk factors to a patient.

“The patient has to decide what their risk is,” explained Gordon. “In other words, if you tell one person they have 25 percent risk for heart attack, they might think that is really high. You can tell another patient and they might say, ‘That is not so bad, that means there is a 75 percent chance that it will not happen.’”

“This perspective is especially important with diseases that may elicit an emotional response like Alzheimer’s disease. Rocky’s case scenario showed that the possible risk to develop Alzheimer’s is 16 percent compared to 9 percent in the general population but this still means that there is an 84 percent chance that he will never develop Alzheimer’s. The concept of risk is pretty far off from the concept of diagnosis and for complex diseases that are caused by multiple genes as well as non-genetic factors, genomic scans *cannot* provide a diagnosis.

“So as genetic counselors we try very hard not to qualify risk; it is really a matter of presenting what your risks are and *then* letting the patient decide if that is high or low. I might start off by asking the patient, ‘What did you think of that risk? Is that high or low and did that create anxiety for you?’ Because if I start off by saying the risk factor is alarming, than the patient might be more alarmed than they would otherwise be.”

### **What Do Genetic Experts Think?**

At his office, Reed E. Pyeritz, M.D., medical genetics division chief in the department of medicine at University of Pennsylvania Health System, took a long look at Rackover’s spit test DNA analysis with the Alzheimer’s disease scenario.

“The only thing in the hypothetical patient report that I saw as worth highlighting is the SNP report on Alzheimer’s



**Reed E. Pyeritz, M.D. chief, Division of Medical Genetics, Department of Medicine University of Pennsylvania Health System.**

disease because that is the only thing that has much power from a statistical sense associated it,” said Pyeritz. “But what is happening is the consumer or the patient is jumping into an area where there are all sorts of potential pitfalls and where you as their health care provider like it or not, have to assume some of the responsibility for interpreting it. I would be the first to admit that there are very, very few primary care providers who are in a position to interpret it.”

So what does Pyeritz think PAs should do with a patient who brings in a spit test DNA analysis?

“What I would say is here is an individual who is very interested in their genetics so this would be an ideal person who you would select to spend quality time with to create a good three-generation family history,” he said. “With it, you will give that person better genetic information at this point in time. And better in the sense of information that they can act upon or you can act upon as their health care provider.

So if once a week you were going to spend time doing a three-generation family history, use that time for the patient who is really interested in genetics.”

However, Pyeritz did conclude that it is essential that PAs take CMEs on genetic and genomic medicine; or go to the NCHPEG (National Coalition for Health Professional Education in Genetics) Web site in an effort to learn the basics of this science.

“All PAs — clinically practicing PAs and PA students — need to know some basics of genetics,” said Matt Dane Baker, a PA and dean of the Philadelphia University School of Science and Health. “The reality is, even though genetics has not totally penetrated clinical practice to the extent that I would have guessed it would have 10 years ago, companies like Navigentics have moved ahead of us. Patients can now get their own DNA scan on their own, and they will come to primary care providers like PAs to help to make sense of it. We as PAs need to learn as much about genetic variations as we can.”



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